PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
8426-1251PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA00/00638	30/05/2000	01/06/1999
International Patent Classification (IPC) or national classification and IPC G01N33/50		
Applicant MERCK FROSST CANADA & CO. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15/12/2000	28.08.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Thumb, W Telephone No. +49 89 2399 7350

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00638

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-43 as originally filed

Claims, No.:

1-18 as originally filed

Drawings, sheets:

1/23-23/23 as originally filed

Sequence listing part of the description, pages:

1-17, filed with the letter of 23.8.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-18
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item I

Basis of the report

Sequence listing pages 1-17, filed with the letter of 23.8.2000 do not form part of the application (Rule 13ter.1(f) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: US-A-5 854 002 (GANT DANIEL B ET AL)
   D2: MELDRUM BRIAN S: 'Update on the mechanism of action of antiepileptic drugs.' EPILEPSIA, vol. 37, no. SUPPL. 6, 1996, pages S4-S11.
   D3: KELLY KEVIN M: 'Gabapentin: Antiepileptic mechanism of action.' NEUROPSYCHOBIOLOGY, vol. 38, no. 3, October 1998 (1998-10), pages 139-144.

2.1 Claim 1 refers to a method for identifying compounds binding to $GABA_B$ receptors, said method comprising the use of gabapentin as a reference substance (positive control).
Assay systems wherein different subunits of GABA receptors (derived from insects) are co-expressed in a host cell, and the ability of a compound to bind to the GABA recognition site is measured, are known in the art (D1, column 4, line 66 - column 5, line 25; column 7, lines 5-13).
However, the prior art does not teach or even fairly suggest to include gabapentin as a reference binding substance in a method for identifying molecules which modify the function of a heterodimer of HG20 and $GABA_BR1a$ or $GABA_BR1b$ by binding to said receptor.
In contrast, the state of the art known to the examining authority teaches that the physiological effects resulting from administration of gabapentin are not based on a direct interaction with GABA receptors (D2, page S8, column 1, paragraph 5;

D3, page 142, column 1, paragraph 3 - column 2, paragraph 2).
It would therefore not be obvious for a skilled artisan to include gabapentin as a reference binding substance in an assay for identifying compounds acting on HG20 and $GABA_BR1a$ or $GABA_BR1b$ heterodimeric receptor.
Claim 1 therefore appears to meet the requirements of Articles 33(2) and 33(3) PCT.

2.2 The same argumentation as put forward above also applies to dependent claim 2 and claims 3-18, the latter all referring to assays for GABA receptor-active agents comprising gabapentin as a reference substance.
Claims 2-18 consequently also appear to comply with the provisions of Articles 33(2) and 33(3) PCT.

Re Item VIII

Certain observations on the international application

1. The term HG20 used throughout the independent claims has no well-recognised meaning in the art and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

2. The term "chimeric HG20 protein" used in claims 2, 4, 6, 8, 10, 12, 15, 17 is vague and unclear and does not clearly define the subject-matter for which protection is sought, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

3. References to the content of prior art documents in the claims (i.e. "Kaupmann et al., 1997, Nature 386:239-46") cannot be allowed as the application should be self-contained (see also PCT Guidelines II-4.17).

4. The dependency of claim 13, referring to claim 6, is not clear (Article 6 PCT) since claim 6 does not relate to a reporter gene.

5. The vague and imprecise statement in the description on page 43, lines 26-30,

implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in a lack of clarity of the claims (Article 6 PCT) when used to interpret them (see also PCT-Guidelines, III-4.3a.).